Clinical and genetic characteristics of patients with hyperinsulinaemic hypoglycaemia diagnosed and treated at a tertiary endocrine center, part of the ENDO-ERN

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Background

Hyperinsulinaemic hypoglycaemia (HH) is a clinically and genetically heterogeneous group of disorders characterized by persistent hypoglycaemia due to inappropriate insulin secretion from the pancreatic β-cell.

Objective

To analyze the demographic, clinical and genetic characteristics of patients with HH, diagnosed and/or treated at a tertiary endocrine center, part of the European reference network on rare endocrine conditions (ENDO-ERN).

Material and methods

- **Medical records of 13 patients (aged 0-11 years) with HH were retrospectively reviewed:**
  - **9 were with congenital hyperinsulinism**
  - **3 patients had transient HH**
  - **1 was with syndromic hypoglycaemia**
- **Data about their demographic, clinical and biochemical characteristics were collected.**
- **Genetic testing was performed in all patients with congenital and syndromic hyperinsulinism.**

Results

- **Ten children (76.7%) were males.**
- **Mean age at presentation was 1.1 ± 3.0 months.**
- **Almost 2/3 of the patients (61.5%) presented at birth having early onset hyperinsulinism.**
- **Four patients (30.8%) were born large for gestational age.**
- **The most common clinical manifestations at presentation were neuroglycopenic symptoms.**

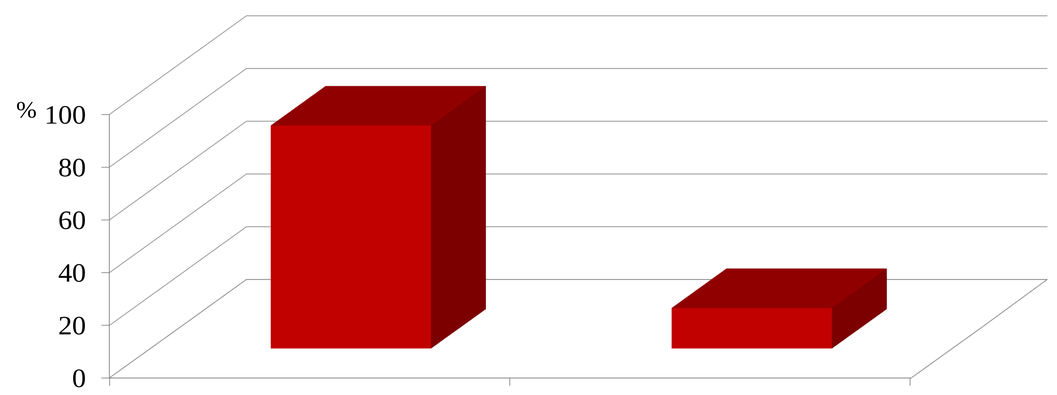
Children with congenital HH

Gender	GA (wg)	Birth weight (g)	Age at onset (m)	Clinical presentation	Gene mutation
F	39	3560	7	Hypotonia Seizures	GLUD1
M	37	3600	At birth	Seizures	ABCC8 Homozygous mutation pGly92Asp
M	38	NA	11	Seizures	No
M	41	3550	7	Hypotonia Seizures	No
M	37	4200	At birth	Seizures	ABCC8 Compound heterozygous mutation pI60N/pG1555V
F	38	2800	7	Seizures	No
M	39	2800	13	Seizures	No
M	38	4660	At birth	Seizures	ABCC8 Heterozygous mutation pE1507K
M	38	2700	At birth	Hypotonia	No

Children with transient/syndromic HH

Gender	GA (wg)	Birth weight (g)	Age at onset (m)	Clinical presentation	Gene mutation
M	39	3760	At birth	Seizures	No
M	37	2480	At birth	Hypotonia cyanosis	No
M	38	2260	At birth	Seizures	No
F	36	2900	At birth	Seizures Hypotonia	11p15.5

Treatment



Genetic testing

- ***ABCC8*** **and** ***GLUD1*** **gene mutations were identified in 44.4% of the children with congenital hyperinsulinism.**
- **One patient was diagnosed with Beckwith-Wiedemann syndrome with a loss of methylation in KvDMR and a gain of methylation in H19 DMR.**

- **More than 92% (12/13) of patients have normal neurological development**
- **Only one patient is with expressive language problems due to diagnostic and treatment delay.**

Conclusion

The majority of hyperinsulinaemic patients have no identifiable mutations, suggesting the role of other genetic and environmental mechanisms.

Since most of the patients present soon after birth, early recognition and prompt treatment are vital in preventing permanent brain damage.

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